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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/897,583	06/29/2001	Thomas A. Szyperski	19226/2051 (R-5655)	1224
7590	05/18/2004			EXAMINER GAKH, YELENA G
Michael L. Goldman NIXON PEABODY LLP Clinton Square P.O. Box 31051 Rochester, NY 14603			ART UNIT 1743	PAPER NUMBER
DATE MAILED: 05/18/2004				

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/897,583	SZYPERSKI, THOMAS A.	
	Examiner	Art Unit	
	Yelena G. Gakh, Ph.D.	1743	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 12/01/03 and the Applicant's request.
 2a) This action is FINAL. 2b) This action is non-final.
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1-132 is/are pending in the application.
 4a) Of the above claim(s) 1-90 is/are withdrawn from consideration.
 5) Claim(s) _____ is/are allowed.
 6) Claim(s) 91-132 is/are rejected.
 7) Claim(s) _____ is/are objected to.
 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
 10) The drawing(s) filed on 29 June 2001 is/are: a) accepted or b) objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>03/04/02</u> . | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. This action is revised in response to the Applicant's request to reconsider pending claims, since claims 131 and 132 were missing from the previous Office action. Also, the on-line references the examiner relied upon in the previous Office action are no longer available in PDF format, which provides the date of their creation. Therefore, new references are applied in the present Office action.
2. Election of claims 91-130 with traverse filed on 12/01/03 is acknowledged. In response to the Applicant's arguments regarding restriction requirements the examiner would like to notice that the NMR experiments listed in claim 91 are not unambiguously defined through particular pulse sequences, and therefore do not define specific NMR techniques. Claim 91 does not refer to the claims of Groups V and VII. Therefore, the restriction requirements are correct and are made FINAL.

Claim 91-132 are pending in the Application.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.
4. Claims 91-132 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for $^{15}\text{N}/^{13}\text{C}$ -labeled proteins, does not reasonably provide enablement for unlabeled proteins. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The pulse sequences recited in the claims require high abundance of ^{13}C and ^{15}N nuclei, which can be provided only in $^{15}\text{N}/^{13}\text{C}$ -labeled proteins, see Szyperski et al. (J. Biomol. NMR, 1998, IDS): “[the protein] isotope labeling becomes mandatory

when ... (ii) the structural refinement shall include heteronuclear scalar coupling constants” (page 140).

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

6. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

7. **Claims 91-102, 131 and 132** are rejected under 35 U.S.C. 103(a) as being unpatentable over Szyperski et al. (J. Biomol. NMR, 1998, IDS) in view of Fernandez et al. (J. Biomol., 1998) or Gehring et al. (JMR, 1998) and Yamazaki et al. (JACS, 1993).

Szyperski discloses “sequential resonance assignment of medium sized $^{15}\text{N}/^{13}\text{C}$ -labeled proteins with projected 4D triple resonance NMR experiments” (Title), comprising performing 3D $\text{H}^{\alpha/\beta}\text{C}^{\omega/\beta}(\text{CO})\text{NHN}$ experiment, 3D HNNCAHA experiment and 3D HNN<CO,CA> experiment for assigning corresponding chemical shifts for the protein backbone.

Szyperski does not specifically disclose using 3D HCCH-COSY and 2D HBCB(CGCD)HD NMR experiments for assigning aliphatic and aromatic side chain chemical shifts.

Fernandez and Gehring disclose side chain assignments based on 2D and 3D HCCH-COSY NMR techniques for assignment of aliphatic side chain chemical shifts for proteins, while

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Yamazaki teaches 2D RD HBCB(CGCD)HD NMR technique for assigning aromatic side chain chemical shifts.

It would have been obvious for anyone of ordinary skill in the art to add two NMR techniques disclosed by Fernandez or Gehring and Yamazaki to the strategy disclosed by Szyperski in order to perform more complete assignment of signals in NMR spectra of proteins by adding assignments for the side chains (aliphatic and aromatic) to the assignment of the protein backbone.

7. **Claims 103-130** are rejected under 35 U.S.C. 103(a) as being unpatentable over Szyperski in view of Fernandez or Gehring and Yamazaki, as applied to claims 91-102, 131 and 132 above, and further in view of Shirra (“Three Dimensional NMR Spectroscopy”, November 28, 1996) or “Cell Cycle/Gene Regulation” protocol, 1998).

Szyperski in view of Fernandez or Gehring and Yamazaki do not specifically disclose some other 3D experiments recited in claims 103-130 for assigning chemical shifts of various backbone and side-chain nuclei of proteins.

Shirra and “Cell Cycle” protocol describe various 3D and 2D experiments for assigning chemical shifts of various nuclei in backbone and side chains of proteins via different pathways, the combination of which leads to complete assignment of NMR spectra, as well as determining protein structure from corresponding NOESY experiments.

It would have been obvious for anyone of ordinary skill in the art to combine various experiments listed in Shirra or “Cell Cycle” protocol, or to modify them in the same way as taught by Szyperski for pulse sequences disclosed by Szyperski in view of Fernandez or Gehring and Yamazaki in order to obtain completely assigned NMR spectra and to determine tertiary structure of proteins from NOE data, since these are the main goals of the cited papers.

Drawings

8. The drawings are objected to because Figure 1 is of a poor quality. A proposed drawing correction or corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.

Conclusion

9. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. *Accelrys* discloses various heteronuclear triple resonance spectra, e.g. 3D: HNCACB + CBCACONH, 4D: HACA(CO)NNH; *Li (Development of an Integrated Software ...*", 1996) discloses algorithms for various 3D NMR experiments; *Nietlispach et al. (JACS, 1996)* disclose "an approach to the structure determination of larger proteins using triple resonance NMR experiments in conjunction with random fractional deuteration"; "*Cell Cycle/Gene Regulation*" (1998) discloses various sequences for assigning protein signals, including HCCTOCSYCONNH (Remark 210); *Sattler (EMBO Practical Course, Sept. 12-19, 2001, publication in Prog. NMR Spectrosc., 1999)* represents a full strategy for assigning NMR spectra and structural determination of proteins; *Kanelis et al. (Life, 2001)* teach "multidimensional NMR methods for protein structure determination".

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yelena G. Gakh, Ph.D. whose telephone number is (571) 272-1257. The examiner can normally be reached on 9:30 am - 6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill A. Warden can be reached on (571) 272-1267. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Yelena G. Gakh

5/14/04

Yelena Gakh